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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/086,087	YANG ET AL.	
	Examiner	Art Unit	
	Stephen Kapushoc	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 September 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1 and 3-8 are pending and examined on the merits.

This Office Action is in reply to Applicants' correspondence of 09/17/2007. Applicants' remarks have been fully and carefully considered but are not found to be sufficient to put the application in condition for allowance. No new grounds of rejection are presented in this Office Action.
This Action is made **FINAL**.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Final Office Action

1. All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Response to Remarks Concerning the Sufficiency of the Declaration

2. Applicants have argued (page 4 of the Remarks of 9/17/2007) that the Declaration submitted under 37 CFR 1.131 is sufficient to establish the conception of the claimed invention on June 5, 2001 by providing a notebook page dated on that date. Applicants' arguments have been considered but are not found to be persuasive.

Applicants have continued to argue, with regard to the phrase 'as shown in Berkeley', that the difference in publishing date of the Shrewsbury et al article and the date on the notebook page has been explained, and that the Declaration in combination with the notebook page and the article are sufficient to show possession of the invention. However, MPEP 715 provides guidance in considering the effectiveness of a Declaration under 37 CFR 1.131 for the purpose of antedating an applied reference. MPEP 715.07 provides:

> The affidavit or declaration must state FACTS and produce such documentary evidence and exhibits in support thereof as are available to show conception and completion of invention in this country or in a NAFTA or WTO member country (MPEP § 715.07(c)), at least the conception being at a date prior to the effective date of the reference.

In the instant case, the Declaration states, in part 8, that 'the reference on the notebook page "as shown in Berkeley" refers to a published article "Effect of Flow on Complex Biological Macromolecules in Microfluidic Devices," by Polly S. Shrewsbury, Susan J. Muller, and Dorian Liepmann and published in 2001 in Biomedical Microdevices, 3:3, 225-238 by Kluwer Academic Publishers'. As pointed out previously by the examiner,

the facts alleged in the Declaration are not consistent with the documentary evidence provided to support the facts. Specifically, it is not possible that the 'as shown in Berkeley' remark, recorded in a notebook on June 5, 2001, can refer to 'a published article' that was published in September of 2001. Applicants have argued that articles are not contemporaneously published upon submission. However, the statement of alleged fact in the Declaration (i.e. part 8) is not a statement that the remark refers to, for example, the method taught in a pre-publication proof or text copy of an article that was later published as the article "Effect of Flow on Complex Biological Macromolecules in Microfluidic Devices," by Polly S. Shrewsbury, Susan J. Muller, and Dorian Liepmann and published in 2001 in Biomedical Microdevices, 3:3, 225-238 by Kluwer Academic Publishers'. Furthermore, the argument of Applicants (i.e. that articles are not contemporaneously published upon submission) is merely an argument, and can not be used to modify the sworn statements of alleged fact presented in the Declaration. Thus, while the Examiner appreciates Applicants arguments, the Examiner must consider the specific statements provided in the Declaration and the documentary evidence when determining the sufficiency of the Declaration to establish a date of possession of the invention as prior to the date of a reference applied under 35 USC 102(e)

While the Examiner appreciates the arguments of Applicants concerning submission and publication of journal articles, the Examiner has explained above the difference between a fact alleged in a Declaration and an argument presented in an effort to modify the facts of a Declaration. In the interest of advancing prosecution in the matter of the date of possession by Applicants of the instantly claimed methods, the

Examiner suggests that Applicants may wish to submit a new Declaration stating the specific facts regarding when and how Applicants were in possession of any information that can properly be accounted for by the remark 'as shown in Berkeley' as referenced on the notebook page, and what that information includes. Applicants may also provide any documentary evidence (e.g. prepublication proofs, documents submitted for publication) to support such statements of fact.

Applicants are reminded of the guidelines for the timely presentation of affidavits or declarations as set forth in MPEP 715.09.

In response to the Examiner's comparison of the requirements of the claims and the provisions of the notebook page and the published article, Applicants have argued that 'an exhibit need not support all claimed limitations provided that the missing material is supported by the Declaration itself'. While the Declaration does not specifically provide any facts regarding the claim limitations as addressed on pages 3-4 of the Office Action of 05/16/2007, it is noted that MPEP 715.03 provides that:

> It is not necessary for the affidavit evidence to show that the applicant viewed his or her invention as encompassing more than the species actually made. The test is whether the facts set out in the affidavit are such as would persuade one skilled in the art that the applicant possessed so much of the invention as is shown in the reference or activity.

In the instant case the claim limitations are supported by the teachings of the notebook page and the published article, though this analysis in no way changes the previous analysis regarding the date of the notebook page and the publication date of the published article.

For the reasons detailed above, the Examiner maintains that the Declaration is insufficient to establish that Applicants conceived the claimed invention as of June 5, 2001.

As noted in the previous Office Action, the Declaration further provides (as Attachment 3) data from 'Invention Tracker' to indicate that diligence was exercised in pursuing a patent application from the time of conception to the time of filing (parts 9-11 of the Declaration). MPEP 715.07(a) provides:

> In determining the sufficiency of a 37 CFR 1.131 affidavit or declaration, diligence need not be considered unless conception of the invention prior to the effective date is clearly established, since diligence comes into question only after prior conception is established. Ex parte Kantor, 177 USPQ 455 (Bd. App. 1958).

Because conception of the invention in a scope commensurate with the requirements of the claims has not been established, the issue of any alleged exercised diligence remains moot.

Maintained Rejections
Claim Rejections - 35 USC § 102

3. Claims 1 and 3-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Bensimon et al (herein referred to as Bensimon), U.S. Patent 6,054,327, 102(b) date 04/25/2000.

Several aspects of instant claim 1 part c) have been broadly interpreted by the Examiner. Passing the hybridized DNA complex "from a reservoir in a microfluidic device" is interpreted as moving any portion of the hybridized DNA complex initially in a holding area in a device designed to contain small amounts of liquids. Passing the hybridized DNA complex through a "narrow channel to cause an acceleration of flow

through said channel" is interpreted as moving any portion of the hybridized DNA complex through a small passageway, which involves an acceleration of flow through the passageway.

Bensimon teaches a method of analyzing DNA comprising hybridizing the DNA in solution with probes having fluorescent reagents and then detecting the position of the probes after aligning ("causing said hybridized DNA complex to extend into a substantially linear configuration", instant claim 1 part c)) the DNA (instant claims 1, 5 and 6; see column 16, lines 50-55, and Fig. 6 of Bensimon). Bensimon also teaches that DNA molecules placed in a channel between cover slips can be aligned by the evaporation flow parallel to a moving meniscus in the channel (instant claim 1 part c); see column 2, lines 11-12 and column 3, line 22 and Fig. 6 of Bensimon). Regarding this method of aligning DNA described by Bensimon, DNA molecules in a random coil state fixed at a location in a channel between cover slips is interpreted as the embodiment of the hybridized DNA complex initially being in a "reservoir in a microfluidic device" as recited in instant claim 1 part c). In addition, as the meniscus initially moves through the channel between the cover slips, there will be an acceleration of fluid flow in the channel and a portion of the DNA complex will pass through the channel as it extends to a linear configuration (see Fig. 6 of Bensimon). This is interpreted as the embodiment of passing the hybridized DNA complex through a "narrow channel to cause an acceleration of flow through said channel, thereby causing said hybridized DNA complex to extend into a substantially linear configuration;" (recited in instant claim 1 part c)). Bensimon teaches that the probes used to hybridize to DNA can be oligonucleotides, RNA, DNA, and peptide nucleic acids (instant claims 5 and 6;

see column 13, lines 21-23 and 64-65 of Bensimon) which identify a specific sequence of DNA by hybridization, and specifically recites the use of multiple probes (which are at least two probes) for the analysis of a DNA molecule (col 13 lns.12-24). Bensimon also teaches that oligonucleotide probes can be labeled with microbeads (instant claims 1, 3 and 4; see column 11, lines 20-41 and column 14, lines 4-7 of Bensimon). With regard to instant claim 1 part d) Bensimon teaches in situ mapping comprising the detection of multiple probes on an aligned DNA molecule (see column 16, lines 50-55 of Bensimon). Relevant to parts e) and f) of claim 1, Bensimon teaches the analysis of the entire length of a linear labeled nucleic acid molecule (e.g. Fig 8) which allows for determining the sequential order of labels on the target, and specifically teaches the use of multiple probes to determine the position or size of multiple specific sequences, which is identification of the target DNA molecule.

Response to Remarks

Applicants have traversed the rejection of claims under 35 USC 102 as anticipated by Bensimon. Applicants argue (pages 5 of Remarks) that Bensimon does not set forth a location of two distinct DNA sequence recognition units on a target DNA in a random coil state. The examiner maintains that the teachings of Bensimon (e.g. col.13-14) provide for hybridizing two or more probes on a DNA in solution, where a DNA in solution as taught in Bensimon is a DNA target in a random coil state. Applicants further argue that there is no teaching of a narrow channel that causes an acceleration of fluid flow. The Examiner maintains that Bensimon meets the broadest reasonable interpretation of the limitations of the claims, where the specification does

not define any structural limitations of, for example, the requirements of a 'narrow channel', and as the meniscus of Bensimon initially moves through the channel between the cover slips, there will be an acceleration of fluid flow in the channel.

The rejection is **MAINTAINED.**

4. Claims 1, and 3-6 are rejected under 35 U.S.C. 102(e) as being anticipated by Chan et al (hereinafter referred to as Chan-1) Pre Grant Publication 2003/0059822, 102(e) date 09/18/2001.

Chan-1 teaches a method of analyzing a polymer comprising labeling the polymer with first and second unit specific makers (thus at least two sequence recognition units, as required by the claims), the first unit specific marker having a first label and the second unit specific marker including a second label distinct from the first label; exposing the labeled polymer to a detection station to produce distinct detection signals from the first and second labels; and identifying the distinct first and second signals (instant claim 1; see page 1, para 0008 of Chan-1). Chan-1 also teaches that the first unit specific marker can be different than the second unit specific marker, either in its nature or in the polymer unit it recognizes and binds to (instant claim 1; see page 1, para 0009 of Chan-1). Relevant to parts e) and f) of claim 1, Chan-1 teaches determining the sequential order of the labels of the labeled target (e.g. Fig 8) and thus determining the order of the specific sequence of the target to identify the target DNA molecule. Chan-1 also teaches that the first unit specific marker can be identical to the second unit specific marker, yet the first and second unit specific markers are labeled

with distinct labels (instant claim 1; see page 1, para 0009 of Chan-1). Chan-1 also teaches that the polymer is preferably a nucleic acid that is genomic DNA (instant claim 1; see page 2, para 0013 of Chan-1) and that the unit specific marker can be a nucleic acid probe (instant claims 5 and 6; see page 8, para 0076 of Chan-1), or a peptide or polypeptide or peptide-nucleic acids (instant claims 5 and 6; see page 8, para 0077 of Chan-1). Chan-1 teaches that unit specific markers are attached to optically distinguishable labels that include a nanoparticlea, colloid gold nanocrystals, and micro beads (instant claims 1, 3 and 4; see page 3, para 0015 of Chan-1). Chan-1 teaches that the pattern of binding of the unit specific markers to the polymer may be determined using a variety of systems including a linear polymer analysis system (instant claim 1; see page 3, para 0033 of Chan-1) such as optical mapping or DNA combing. Chan-1 teaches that the unit specific marker (and thus the polymer) can be sequentially exposed to a station, "station" defined as a region where a portion of the polymer is exposed to an energy source in order to produce a signal or polymer dependent impulse, by movement of the marker and the station relative to one another (instant claim 1; see page 12, para 0109 of Chan-1). Chan-1 teaches that the polymer can be aligned and stretched before it reaches the interaction station and that a very effective technique of stretching DNA is to pass the polymer through a tapered microchannel having an obstacle field, followed by a constant-shear section to maintain the stretching obtained and straighten out any remaining coiling in the polymer (embodiment of "passing said hybridized DNA complex" in instant claim 1 part c); see page 13, para 0125 and page 14, para 0128 of Chan-1). Chan-1 also teaches that pressure flow is the

preferred driving force of the DNA through such a microchannel recited above (see page 14, para 0128 of Chan-1). With regard to instant claim 1 part d), Chan-1 teaches detecting optically distinguishable DNA sequence recognition units in a sequential manner along a substantially linear hybridized DNA complex (see page 1, para 0008 and page 3, para 0033 of Chan-1, also Figure 2).

Response to Remarks

Applicants have traversed the rejection of claims under 35 USC 102(e) as anticipated by the teachings of Chan-1. Applicants argue (page 6 of Remarks) that Chan-1 analyzes a polymer by providing markers on the polymer, whereas the instant invention is a method where a single molecule identification is carried out by attaching optically distinguishable material to a DNA sequence recognition unit that identifies a specific sequence of DNA. This argument has been considered but is not found to be persuasive. The teachings of Chan-1 (p.8 ¶76 and ¶81; Figure 2) specifically include that the unit specific markers may be nucleic acid probes (as taught by the instant specification). The analysis of Chan-1 utilizing nucleic acid probes to analyze a nucleic acid polymer is a method that identifies the nucleic acid polymer at least in so far as the method identifies the order and location of probes bound to the polymer.

The rejection as set forth **is MAINTAINED.**

5. Claims 1, and 3-8 are rejected under 35 U.S.C. 102(e) as being anticipated by Hannah et al (hereinafter referred to as Hannah; U.S. Patent 6,767,731 B2, 102(e) date 08/27/2001).

Hannah teaches a method of sequencing a target nucleic acid comprising hybridization of the target DNA with probes, which can be oligonucleotides and oligonucleotide analogs that are uniquely and detectably labeled, using a microfluidic device to pass the hybridized nucleic acid through a microchannel to extend it to an approximate linear conformation by hydrodynamic focusing, and detecting the spectral signature of each labeled probe (thus teaching multiple probes, which includes at least two probes), preferably in sequential order (instant claims 1, 5 and 6; see column 2, lines 38-44 and 51-56, and column 3, lines 3-7 and 9-11 of Hannah). Relevant to parts e) and f) of claim 1, Hannah teaches that the labels of multiple probes may be detected in a linear fashion (thus sequential detection) to determine the probe order and identify the target DNA molecule (col.17 – Example 3). Hannah also teaches that nucleic acid molecules sequenced by this method can be DNA or RNA (instant claim 1; see column 4, lines 62-65 of Hannah). Hannah also teaches that the probes used for this method can be DNA, RNA, or analog thereof, such as a peptide nucleic acid (instant claims 5 and 6; see column 6, lines 30-34 of Hannah). Hannah also teaches that the probe labels can be fluorescent, luminescent, radioactive, phosphorescent, chemiluminescent, enzymatic, spin, electron dense, mass spectroscopic, semiconductor nanostructures, and quantum dots (instant claims 2-4; see column 8, lines 42-47 and column 10, lines 12-37 of Hannah). Hannah also teaches that photolithography can be used to obtain microchannels for use in linearizing DNA in the range of tens of micrometers wide and deep (instant claims 7-9; see column 12, lines 14-16 of Hannah). With regard to instant claim 1 part d), Hannah teaches analyzing the linear order of probes on a target nucleic

acid where each probe has a distinct spectral signature (see column 2, lines 38-44 and 51-56, and column 3, lines 3-7 and 9-11 of Hannah).

Response to Remarks

Applicants have traversed the rejection of claims under 35 USC 102 as anticipated by Hannah. Applicants argue (p.7 of Remarks) that Hannah teaches probes that are detectable only upon exposure to an electron beam, which is in contrast to the instantly claimed methods requiring optically distinguishable colored microparticles. This argument is not found to be persuasive. Hannah teaches probes labeled with a variety of markers, including fluorophores and xanthene dyes. While it is true that such dyes are detectable by their emission of a particular wavelength of light upon excitation by a particular wavelength of light, this is not to say that such dyes are not colored, or optically detectable. For example, the detection of any element by optical means requires light; for example if one were to label a probes with a colored microparticle in an environment with no light, one would not drawn the conclusion that the microparticle is not optically detectable. Furthermore, the specific dyes taught by Hannah include dyes that are visible upon exposure to visible light, where in light of the particular teachings of the specification that "optically distinguishable materials which can be used in the invention include, for example, colored microparticles, such as, dyes, dye aggregates, pigments or nanocrystals" supports the application of the labels of Hannah in satisfying the limitations of the claims.

The rejection is **MAINTAINED.**

Maintained Rejections
Claim Rejections - 35 USC § 103

6. Claims 7 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chan-1 Pre Grant Publication 2003/0059822, in view of Chan-2 et al (PCT/US00/22253, International Publication Number WO 01/13088 A1).

Chan-1 teaches a method of analyzing a polymer comprising labeling the polymer with first and second unit specific makers (thus at least two sequence recognition units, as required by the claims), the first unit specific marker having a first label and the second unit specific marker including a second label distinct from the first label; exposing the labeled polymer to a detection station to produce distinct detection signals from the first and second labels; and identifying the distinct first and second signals (instant claim 1; see page 1, para 0008 of Chan-1). Chan-1 also teaches that the first unit specific marker can be different than the second unit specific marker, either in its nature or in the polymer unit it recognizes and binds to (instant claim 1; see page 1, para 0009 of Chan-1). Relevant to parts e) and f) of claim 1, Chan-1 teaches determining the sequential order of the labels of the labeled target (e.g. Fig 8) and thus determining the order of the specific sequence of the target to identify the target DNA molecule. Chan-1 also teaches that the first unit specific marker can be identical to the second unit specific marker, yet the first and second unit specific markers are labeled with distinct labels (instant claim 1; see page 1, para 0009 of Chan-1). Chan-1 also teaches that the polymer is preferably a nucleic acid that is genomic DNA (instant claim 1; see page 2, para 0013 of Chan-1) and that the unit specific marker can be a nucleic acid probe (instant claims 5 and 6; see page 8, para 0076 of Chan-1), or a peptide or

polypeptide or peptide-nucleic acids (instant claims 5 and 6; see page 8, para 0077 of Chan-1). Chan-1 teaches that unit specific markers are attached to optically distinguishable labels that include a nanoparticles, colloid gold nanocrystals, and micro beads. Chan-1 teaches that the pattern of binding of the unit specific markers to the polymer may be determined using a variety of systems including a linear polymer analysis system (instant claim 1; see page 3, para 0033 of Chan-1) such as optical mapping or DNA combing. Chan-1 teaches that the unit specific marker (and thus the polymer) can be sequentially exposed to a station, "station" defined as a region where a portion of the polymer is exposed to an energy source in order to produce a signal or polymer dependent impulse, by movement of the marker and the station relative to one another (instant claim 1; see page 12, para 0109 of Chan-1). Chan-1 teaches that the polymer can be aligned and stretched before it reaches the interaction station and that a very effective technique of stretching DNA is to pass the polymer through a tapered microchannel having an obstacle field, followed by a constant-shear section to maintain the stretching obtained and straighten out any remaining coiling in the polymer (embodiment of "passing said hybridized DNA complex" in instant claim 1 part c); see page 13, para 0125 and page 14, para 0128 of Chan-1). Chan-1 also teaches that pressure flow is the preferred driving force of the DNA through such a microchannel recited above (see page 14, para 0128 of Chan-1). With regard to instant claim 1 part d), Chan-1 teaches detecting optically distinguishable DNA sequence recognition units in a sequential manner along a substantially linear hybridized DNA complex (see page 1, para 0008 and page 3, para 0033 of Chan-1, also Figure 2).

Chan-1 teaches stretching DNA by passing the DNA through a microchannel, but is silent with respect to the width or depth of the channel (see page 13, para 0125 and page 14, para 0128 of Chan-1).

Chan-2 teaches that a channel with 1 μm depth, 1 mm length, and a shear rate of 0.25/s gives a force of approximately 0.25 pN, which the inventors have verified experimentally is adequate to stretch DNA (instant claims 7 and 8; see page 25, line 16 of Chan-2).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to perform the method of Chan-1 with the device of Chan-2 because Chan-2 specifically teaches a device for performing the method of Chan-1. The ordinary artisan would have been motivated to use the device of Chan-2 because Chan-1, while generally teaching a method of stretching DNA with a microfluidic device, is silent with regard to the specific structure and dimensions of the device. The device, with its specific dimensions, taught by Chan-2 functions to stretch DNA as taught by Chan-1. The ordinary artisan would be motivated to use the device of Chan-2 in the method of Chan-1 because Chan-1 teaches to stretch DNA by passing the DNA through a microchannel, but no specific structure or dimensions of the microchannel are recited.

Response to Arguments

Applicants have traversed the rejection of claims under 35 USC 103 as obvious in view of the teachings of Chan-1 in view of Chan-2. Applicants (p.8 of Remarks) reiterate the arguments regarding the teachings of Chan-1 as drawn to a method of analyzing a polymer by providing markers on the polymer whereas Applicants assert

that the instant invention is a method of identifying a target DNA molecule. This argument with regard to the teachings of Chan-1 has been addressed previously in this Office Action. Applicants further argue that there is no teaching in Chan-2 teaching to label DNA molecules. However, Chan-2 does teach the labeling of DNA molecules (for example the labeling of target molecules in Examples 1 and 2 on pages 43-47). It is noted that Chan-1 provides teachings of the labeling of a DNA sequence recognition unit and the hybridization of DNA sequence recognition units to a target DNA molecule.

The rejection as set forth is **MAINTAINED**.

7. Claims 1, 3 and 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chan et al PCT/US00/22253 (WO 01/13088 publication date 02/22/2001, herein referred to as Chan-2) in view of Bensimon et al (U.S. Patent 6,054,327).

Chan-2 provides methods for the sequence analysis of a single nucleic acid molecule by visual examination of a nucleic acid molecule stretched into a linear conformation.

Chan-2 teaches (e.g. page 22) methods comprising extrinsically labeling a target nucleic acid sequence using an oligonucleotide (which is a DNA sequence recognition unit that identifies a specific sequence of DNA in a target, termed in the reference a 'unit specific marker') to which a label such as a fluorescent dye (which is an optically distinguishable material) is attached, relevant to part a) of claim 1. Relevant to part b) of claim 1, Chan-2 teaches that a labeled oligonucleotide can be hybridized to a target DNA to 'mark' a specific target sequence in the target (e.g. page 22), teaches that any

particular target DNA may be hybridized to more than one marker (p.23 lns.3-6), and teaches the target DNA may be 'marked' when it is in a random coil state (e.g. page 45). Relevant to part c) of claim 1, Chan-2 teaches passing the labeled target DNA through a channel in a fluid carrier to cause the target:label complex to extend into a linear conformation (e.g.: p.39 ln.30; p.45 Example 6.2; Figs 9 and 15), and that the effect of accelerated fluid flow causes the target DNA to extend (e.g.: p.29 - Branched Channels; p.27 – Funnel Structures). Relevant to part d) of claim 1, Chan-2 teaches the detection of the labels on the target DNA along the length of the target (e.g. Figs 26-28; p.45 lns.1-11) thus allowing for the sequential detection of the label. Relevant to parts e) and f) of claim 1, Chan-2 teaches that the method can be used to analyze polymers to determine polymer sequence (e.g. p.22 lns.28-33), which is a determination of the sequential order of the labels of the DNA sequence recognition unit thereby identifying the target DNA molecule.

Chan-2 does not specifically teach the labeling of oligonucleotide probes with microparticles.

Bensimon teaches methods for the analysis of linearized target nucleic acid molecules using oligonucleotide probes, and teaches that oligonucleotide probes can be labeled with fluorescent labels and microbeads (instant claims 2-4; see column 11, lines 20-41 and column 14, lines 4-7 of Bensimon).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the oligonucleotide labeling techniques taught by Bensimon et al to analyze oligonucleotide probes hybridized to target DNA

molecules in the methods of Chan-2. One would have been motivated to use the techniques of Bensimon et al based on the assertion of Bensimon that such methods are suitable for the detection of probes hybridized to a single target DNA molecule stretched into a linearized conformation.

Response to Remarks

Applicants have traversed the rejection of claims under 35 USC 103 as obvious over the teachings of Chan-2 in view of Bensimon. Applicants reiterate the argument (p.9 of Remarks) that Bensimon fails to disclose formation of a molecule that has been hybridized to at least two distinct DNA sequence recognition units when the DNA is in a random coil state. This argument has been addressed previously in this Office Action where the teachings of Bensimon (e.g. col.13-14) provide for hybridizing two or more probes on a DNA in solution, where a DNA in solution as taught in Bensimon is a DNA target in a random coil state.

The rejection as set forth is **MAINTAINED.**

Conclusion

8. No claims are allowed.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Kapushoc whose telephone number is (571)272-3312. The examiner can normally be reached on Monday through Friday, from 8am until 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Stephen Kapushoc
Art Unit 1634

/Jehanne S Sitton/
Primary Examiner, Art Unit 1634